REMARKS

Applicant notes from the current Office Action that all prior grounds of rejection under 35 USC 112 and 35 USC 102 have been withdrawn and that the only substantive ground of rejection now pending is a new rejection under 35 USC 103(a) over substantially the same prior art that was previously used in the rejection under section 102.

Before we look at the specifics of the rejection over prior art, it should be appreciated that the present invention is not and does not claim to be the only technique for establishing a maximum therapeutic dose for a radiopharmaceutical. Such techniques exist and have existed for years. Instead, the invention *as claimed* is directed to a *specific improvement* using a modification of the relatively new concept of "lean body mass" that was originally developed in the laboratories of some of the current inventors, namely Wahl and Zasadny. Specifically, the present invention is *an improvement of an improvement*, as the present invention is an improvement over the earlier invention described in the cited prior art references, namely WO 9634632 by Wahl and Zasadny and their corresponding issued U.S. patent, namely USP 6,251,362 (collectively the "earlier Wahl and Zasadny publications"), which was itself an improvement over earlier techniques. The earlier Wahl and Zasadny publications describe the initial method developed for calculating a patient specific dose of a radiolabeled pharmaceutical using a "lean body mass" concept, while the present invention is an improvement of the earlier technique.

To this extent, the earlier Wahl and Zasadny publications and the present invention are "related," as the present invention also *begins* with the concept of lean body mass. However, the two techniques are not identical, and there is nothing in the earlier Wahl and Zasadny publications to point anyone toward the specific differences that are recited in the second technique. In fact, calculations for the same patient using the two different techniques lead to two different recommended doses, especially for obese patients. The earlier technique, for example, uses a comparison between "actual body mass" and "*lean body mass*" to provide a more accurate dose calculation for obese patients than had been previously available. The current technique uses a comparison between "actual body mass" and "*maximum effective mass*," with "maximum effective

mass" being under the conditions exemplified in the specification1.37 times the value of "lean body mass" (see pages 12 and 13 of the current specification). Furthermore, that the present technique provides advantages over the prior technique surely cannot be questioned, as the current process is the only one of the two that has been approved by the FDA for use with actual patients (discussed further below).

As a result of specific differences like this, the two calculation techniques provide different results (especially for obese patients) that can make a life or death difference when the two techniques are used to calculate the therapeutic dose that a patient will receive. To better show these differences, the inventors have prepared a series of calculations for a hypothetical patient, and a copy of the calculation is shown in Appendix A. This particular example is in three parts and shows (1) the suggested therapeutic dose (104.4 mCi) for a hypothetical patient when calculated by the method shown in the earlier Wahl and Zasadny publications, (2) the suggested therapeutic dose (130.7 mCi) for the method as currently claimed when calculated using equations set out in the current specification, and (3) the suggested therapeutic dose (138.8 mCi) for the method as currently claimed when calculated using a graphical estimation technique set out in the current specification. The appendix concludes with a brief summary of the results in tabular form.

Since the goal of any calculation of this type is to provide the highest possible safe dose ("highest possible" so that the chances of curing the patient's cancer are highest) and since this techniques has been approved by the FDA as being safe, the advantages of the present invention are apparent. That the advantages are unobvious is also clear, since the earlier Wahl and Zasadny publications purported to provide the highest possible safe dose, while the doses provided by the present method are higher (and thus likely to be more effective in treating cancer) while still being safe.

So that the Examiner can understand that the method claimed in the current application is the method recently approved by the FDA, applicant includes a copy of the label instructions for a pharmaceutical now on the marker that received approval from the FDA on June 27, 2003. If the Examiner would like to verify these label instructions, an official copy can be found on the internet at the following URL (an FDA website):

http://www.fda.gov/cber/label/tosicor062703LB.pdf.

The description of the dosimetry methodology is spread throughout the text of the label instructions (which are obviously designed for uses other than in the USPTO), but a good summary relevant to the claims appears beginning at line 912 of page 34, where steps are set out that mirror many of the specific steps of claim 1 of the current patent application. Note line 932, for example, that calls for a "Maximum Effective Mass," the measure used in the present invention (and not a "lean body mass" as called for in the earlier Wahl and Zasadny publications). Also note the specific formula that appears at line 942 on page 35. This formula is from the present application, not the earlier Wahl and Zasadny publications, and appears in claim 1.

The Examiner is invited to calculate as many further examples as she desires, and such additional calculations are specifically requested if there is any belief on the part of the Examiner that the two techniques provide "obvious" results or are "obvious" variations of each other. It is applicant's position that obese patents would be prescribed significantly higher doses for the current technique relative to the therapeutic doses that would be prescribed for the technique shown in the earlier Wahl and Zasadny publications, and that such higher doses cannot be considered to be obvious in view of the earlier Wahl and Zasadny publications' stated desire to provide the "optimal" dose.

Although not precisely so stated in the Office Action, perhaps the current rejection is based on a belief that the phrase "maximum effective mass" (or some other phrase) inadvertently reads on some aspect that is similar (such as "lean body mass") in the earlier Wahl and Zasadny publications. So that this issue can be fully considered, applicant submits two new claims based on specific language found in the specification on page 13 where "maximum effective mass" is described in detail. Claim 85 provides that the maximum effective mass is a multiple of a calculated lean body mass, while claim 86 names the multiple as 1.37. Consideration of these specific claims (and of this specific issue) is requested.

Conclusion

If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned at (650) 843-5070. The undersigned believes that an interview would be helpful in the

event that the Examiner believes the two methods to be different but further believes that the current wording is not sufficiently clear to distinguish the methods, and such an interview (by telephone) prior to the issuance of any further office action other than an allowance is requested.

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Respectfully submitted,
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